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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,126	07/17/2003	Joseph M. Jacobson	034474-0106	2592

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EXAMINER	
LUNDGREN, JEFFREY S	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 04/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,126	JACOBSON ET AL.	
	Examiner	Art Unit	
	Jeff Lundgren	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) 1-37, 43-50 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *see office action*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election of Invention and Status of the Claims

Applicant's election without traverse of Group III, claims 38-42, in the reply filed on December 29, 2005, is acknowledged.

Claims 1-50 are pending in the application, claims 38-42 are being examined on the merits and claims 1-37 and 43-50 are withdrawn.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on December 8, 2003, has been considered by the Examiner. The submission is in compliance with the provisions of 37 CFR § 1.97. Enclosed with this Office Action is a return-copy of the Form PTO-1449 with the Examiner's initials and signature indicating those references that have been considered.

Objection to the Abstract Under 37 C.F.R. § 1.72

The abstract of the disclosure is objected to because it does not allow the public generally to determine quickly from a cursory inspection the nature and gist of the invention. Applicants should amend the abstract so that it corresponds to at least one independent claim. For example, Applicants should describe each of the components of their molecular assembly line, such as the molecular chain, the shuttle, the assembly molecule, and the one or more building blocks, as well as their relationship and function as it pertains to the claimed invention. *See* 37 C.F.R. § 1.72. Should Applicants amend the claims in their next reply, the amended abstract should take into account any further limitations added to the broadest independent claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-42 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, Applicants do not have written description support for the claimed subject matter.

The written description requirement is distinct from the enablement requirement; this was first pointed out by the court in *In re Ruschig*, 379 F.2d 990, 154 USPQ 118 (CCPA 1967), and clarified in *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d 1111 (Fed. Cir. 1991). The issue of whether the claimed subject matter is adequately supported/described by the specification, is a question of *fact*. *Id.* at 1563, 19 USPQ2d at 1116.

When considering whether the claimed subject matter complies with the written description requirement, Applicants' disclosure should be read in light of the knowledge possessed by those skilled in the art.

> "[T]he disclosure in question must be read in light of the knowledge possessed by those skilled in the art, and that knowledge can be established by affidavits of fact composed by an expert, and by referencing to patents and publications available to the public..."

In re Lange, 644 F.2d 856, 863, 209 USPQ 288, 294. *See also, In re Alton*, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996).

Applicants enjoy the presumption that their patent application is valid and all statements contained therein are accurate; it is the PTO's burden to demonstrate why any of Applicants claims should be rejected or why any of Applicant's statements should be doubted.

> "it is incumbent upon the Patent Office, whenever a rejection... is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure."

In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 370. If successful in presenting such evidence and argument, the burden then shifts to the Applicant to provide evidence that would convince one to the contrary.

The Invention in General

A significant component of Applicants' invention is directed to a molecular assembly line capable of controlling the binding of certain molecular units, controlling certain chemical reactions at a given molecular assembly site, applying an input signal and causing a nanoscale movement or shift in the molecule, and applying another chemical reaction for adding a subsequent molecular unit onto the molecule.

Accordingly, such an invention requires a device that is capable of controllably moving molecules in a desired manner with nanoscale and/or angstrom-level precision. The claimed invention also requires the ability to apply energy inputs on the order of magnitude of a chemical bond at a given molecular region *via* the use of Applicants' assemble line, and then to chemically react a subsequent molecular unit onto the substrate at the desired location.

The Supporting Disclosure

Applicants describe in their specification how molecular "shuttles" have been studied in recent years, but note that a molecular assembly line has yet to be constructed (pages 1 and 2). Applicants further list a number of embodiments of the claimed invention and certain components utilized (pages 3-4).

A generalized description of the invention components is listed, and certain embodiments, and certain operational aspects are noted (pages 7-11). Applicants summarize their figures and list certain elements as they pertain to the claimed invention (11-28).

For examples, Applicants have an example of selective dehybridization (*i.e.*, a shuttle, not an assembly line; pages 28-32), and an illustration of certain photochemical cleavage reactions (pages 32-35). There is ***no working example*** of the claimed invention, *i.e.*, the molecular assembly line.

Written Description Decisions from the Federal Circuit and CCPA

Certain cases that deal with the written description requirement include *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997), hereinafter "*Lilly*," *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 956, 63 USPQ2d 1609 (Fed. Cir. 2002), hereinafter "*Enzo II*," which was reheard by the Federal Circuit following the original

holding in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013, 62 USPQ2d 1289 (Fed. Cir. 2002), hereinafter "*Enzo I*"; *In re Wallach*, 378 F.3d 1330, 71 USPQ2d 1939 (Fed. Cir. 2004), hereinafter "*Wallach*," and *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 69 USPQ2d 1886, hereinafter "*Rochester.*"

In the case of *Rochester*, the University filed a patent application having disclosure generally related to the art for the selective inhibition of certain cyclooxygenases using NSAID. It was understood in the art that two closely related cyclooxygenases, COX-1 and COX-2, although structurally similar, were physiologically distinct. COX-1 was determined to be expressed in the gastrointestinal tract and found to be important in protecting the stomach lining, whereas COX-2 was determined to be responsive to inflammatory stimuli and associated with arthritis. Accordingly, certain non-selective COX-inhibitors, such as aspirin and ibuprofen which bind both COX-1 and COX-2, are able to treat symptoms of arthritis but are known to cause mild to severe stomach irritation. With this understanding in mind, Rochester recognized the value in developing a screening assay for determining whether a particular compound possessed the ability to selectively inhibit COX-2 over COX-1.[1] *Rochester*, 358 F.3d at 917-918.

The University filed a patent application and obtained a patent directed to a method "for *identifying a compound* that inhibits prostaglandin synthesis catalyzed by mammalian prostaglandin H synthase-2 (PGHS-2)." *Id.* 358 F.3d at 918, emphasis added. The University later filed a divisional application from the aforementioned application, which was eventually allowed, and issued as U.S. Patent No. 6,048,850 ("the '850 patent), having representative claim 1 as follows:

> 1. A method for selectively inhibiting PGHS-2 activity in a human host, comprising *administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product* to a human host in need of such treatment.

Id. 358 F.3d at 918, emphasis added.

Upon issuance of the '850 patent, the University brought suit against a number of defendants (collectively referred to as "Pfizer") for patent infringement in the United States

[1] COX-1 and COX-2 are alternatively referred to as "PGHS-1" and "PGHS-2," respectively, where "PGHS" is an abbreviation for "prostaglandin H synthase."

District Court for the Western District of New York. Rochester alleged that the sale of Pfizers' COX-2 inhibitors CELEBREX™ and BEXTRA™ for treatment of inflammation infringed certain claims in the '850 patent. Pfizer moved for summary judgment of invalidity of the '850 patent for failure to comply with the written description requirement; Rochester opposed, and filed a cross-motion on the issue of written description. *Id.*, 358 F.3d at 919.

In evaluating the parties' motions, the district court found that, although the '850 patent claims require the use of a "non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product," the '850 patent does not disclose such a compound, nor the means to obtain such a compound; the court concluded that "[w]ithout such a compound, it is impossible to practice the invention." *Id.*, 358 F.3d at 926. The Federal Circuit affirmed.[2]

On appeal, the University presented certain arguments as to why the district court erred in its decision of invalidity for failure to satisfy the written description requirement. Of special note is the University's reliance on *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989 (Fed. Cir. 2000) ("Unocal"). Rochester argued:

> "[C]onsistent with written description's fact-intensive nature, this Court has recognized diverse forms of description, including description primarily (if not entirely) based on functional characteristics. In [Unocal], for example, the Court rejected the argument that the patent-in-suit was invalid because it described claimed gasoline mixtures by their "desired characteristics," rather than by their "exact chemical component[s]."

Rochester, 358 F.3d at 926. However, the court was not persuaded, and explained that the range of properties of the claimed gasolines were consistent with the refinery art, and that the Unocal disclosure provided an adequate written description:

> "Evidence was adduced in [Unical] that *artisans skilled in petroleum refining were aware of the properties of raw petroleum sources and knew how to mix streams of such sources to achieve a final product with desired characteristics.* Accordingly, we held that the written description requirement was satisfied in that case by specifying the ranges of properties of the claimed gasolines, *reflecting the way that oil refiners*

[2] The district court also found that the claims in the '850 patent were also not enabled. However, unlike the decision in *In re Fisher*, Case no. 04-1465, decided by the Fed. Cir. on September 5, 2005, wherein the Court ruled that the Fisher invention lacked both utility *and* enablement, the Federal Circuit considered the enablement issue of *Rochester* to be moot in view of the holding that the claims lacked written description, and did not discuss the issue further. *Rochester*, 358 F.3d 929-930.

> *actually formulate gasoline*, such that one skilled in the art could recognize what was being claimed. *Id.* at 992. *The present case is not analogous.* Rochester did not present any evidence that the *ordinarily skilled artisan [in the biotechnology arts]* would be able to identify any compound based on its vague functional description as "a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product."

Id. 358 F.3d at 928, emphasis added. Based on the differences between the state-of-the-art in the petroleum refining arts and the pharmaceuticals arts, the Court distinguished *Unocal* from the holding in *Rochester*, and found that "the how and which" characteristics can be claimed is determined by the facts, and is taken on a case-by-case basis.

Neither did the Court find persuasive the University's reliance and arguments based on *In re Edwards*.[3] *Rochester*, 358 F.3d at 928. In *Edwards*, the claim at issue (which stood rejected for lack of written description by the Board of Patent Appeals and Interferences), was directed to a water-insoluble polyol having the property of self-catalyzing reaction with organic polyisocyanates to form rigid polyurethane foam, wherein the polyurethane was claimed by a generic chemical formula. *Edwards*, 196 USPQ at 466. However, the CCPA found that "as a factual matter," and "taken as a whole," one of ordinary skill in the art would have found that the Edwards application had sufficiently described the claimed compounds. *Id.* 196 USPQ at 469-470. To the contrary, the Court in *Rochester* noted, that the '850 patent does not contain any disclosure for making even a single compound. *Rochester*, 358 F.3d at 928. For at least these reasons, the Court determined that the University had failed to satisfy the written description requirement.

The State of the Art

As it is with many biotechnology inventions, the relevant art is multidisciplinary. Applicant's claimed invention relates to a number of core technologies and scientific concepts including nanopatterning and controllably moving molecules on the nanoscale *via* controllable inputs/forces. Accordingly, those of skill in the art have a firm understanding of the inter-relationship between each of the disciplines and the functional and physical limitations of the claimed invention, and is pertinent in determining the level of skill in the art. Taken as a whole,

the relevant art suggests that Applicant was neither in possession nor had written description support for the claimed invention at the time the application was filed.

The cited references raise a number of factual considerations that reasonably challenge Applicant's disclosure, and would lead one of ordinary skill in the art to doubt that Applicant had adequately described the claimed molecular assembly line.

In general, one major obstacle in constructing Applicants' claimed assembly line is the required atomic resolution for surface immobilized components, such as DNA. For example, each of Ge and Demers illustrate that current methods of construction do not reach the angstrom level of precision required by Applicants' assembly line (Ge *et al.*, *Biosensors and Bioelectronics 18*:53-58 (**2000**), and Demers *et al.*, *Science 296*:1836-1838 (**2002**)). See each of the figures in Ge and Demers, and note that the molecular resolution is not even on the nanometer or angstrom level scale.

Another significant obstacle concerns the controlled movement required by Applicants' device. For example, Applicants suggest that they can control dissociation and association reactions of neighboring molecular sites, and thereby shift a substrate molecule down the chain by a single molecular unit. Applicants allege that a component of this may involve the use of, for example, an optical probe (page 16, paragraph 0059). However, numerous dye molecules are routinely excited and do not cause the effects identified by Applicants, for example, as in Hamad-Schifferli (see Figure 3 and description thereof, Hamad-Schifferli *et al.*, *Nature 415*:152-155 (**2002**)). Further, Hamad-Schifferli shows that molecules can be removed, but does not show the "shifting" as claimed by Applicants. This would require the ability to apply just enough force to cause dissociation at one given site, and at a neighboring site apply a force to cause association, all occurring on the time scale of diffusion over molecular distance (sub-nanosecond for these distances). Applicants' disclosure hardly takes into consideration the highly intricate considerations of these factors.

Generally, there is a reasonable level of doubt that would suggest that Applicant's has not met the written description requirement. Applicants do not provide a description that reasonably overcomes the factual understanding that is indicative of the state of the art. The greater part of

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[3] *In re Edwards*, 568 F.2d 1349, 196 USPQ 465 (CCPA 1978) ("Edwards").

the claimed invention relies on oversimplified illustrations that significantly omit practical real world physicochemical considerations as cited above. One of skill in the art would find these factors essential in considering the practical application for creating and using such an assembly line.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 38, 39, and 41, are rejected under 35 U.S.C. 102(b) as being anticipated by Guatelli *et al.*, *Clinical Microbiology Reviews 2*:217-226 (**1989**).

Applicants invention reads on an active DNA polymerase for the reasons explained below; Guatelli teaches operational polymerase (see Figures 1 and 2, and description thereof).

Claim 38 is directed to an "assembly line" comprising two or more molecular subunits connected to form a chain (the DNA template), a shuttle (the polymerase), an assembly molecule (the next nucleotide to be attached by the polymerase), and one or more building blocks disposed along the molecular chain (certain other nucleotides in the chain); the polymerase moves along the chains attaching subsequent building blocks in response to one or more input signals (*i.e.*, binding of the chemical elements). Claim 39 requires nucleotides, as taught by Guatelli; claim 41 requires a solution reaction, which is also taught by Guatelli.

Claims 38-42 are rejected under 35 U.S.C. 102(a) as being anticipated by Hamad-Schifferli *et al.*, *Nature 415*:152-155 (**2002**).

Claim 38 is directed to an "assembly line" comprising two or more molecular subunits connected to form a chain, a shuttle, an assembly molecule, and one or more building blocks

disposed along the molecular chain; the polymerase moves along the chains attaching subsequent building blocks in response to one or more input signals.

Hamad-Schifferli teaches the claimed invention, as illustrated by Figure 2. The requirement of the shuttle moving between binding positions is met by the fact that the shuttle of Hamad-Schifferli must diffuse through solution and align itself on the other strand of DNA.

The assembly molecule and molecular building blocks are DNA, as required by claim 39; the shuttle comprises a bead (gold bead in Figure 2), as required by claim 40. The assembly line is in solution as required by claim 41. The shuttle may move/diffuse bi-rectionally, as required by claim 42.

Conclusions

If Applicants should amendment the claims, a complete and responsive reply will clearly identify where support can be found in the disclosure for each amendment. Applicants should point to the page and line numbers of the application corresponding to each amendment, and provide any statements that might help to identify support for the claimed invention (*e.g.*, if the amendment is not supported *in ipsis verbis*, clarification on the record may be helpful). Should Applicants present new claims, Applicants should clearly identify where support can be found in the disclosure.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Jeff Lundgren whose telephone number is 571-272-5541. The Examiner can normally be reached from 7:00 AM to 5:30 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JSL

JON EPPERSON, PH.D.
PATENT EXAMINER